

## The ovarian transplant debate

Ovarian tissue auto-transplantation is used when a young woman is facing genito-toxic therapy for cancer. The process of removing healthy ovarian tissue, cryopreserving the sample and re-implanting it at a later date has proven value in allowing fertility in patients otherwise facing a childless future ([Diaz et al](#) *Front Endocrinol* 2022 doi 10.3389/fendo.2022.918899).

The question of using this technology to delay the onset of a naturally occurring menopause is not fantastical since it has already been initiated “in carefully selected candidates”. To date about 20 such patients are known to have accepted the procedure with a view to later using their own ovarian tissue transplantation (OTT) to postpone their menopause ([Vargas Medscape](#) 2024). The doctors at the clinic offering this service have published a schematic forecast giving projections of how to estimate the number of years whereby the menopause transition can be “put-on-hold”, depending on the age of the initial harvesting, the woman’s ovarian reserve and cryopreservation technology ([Johnson et al](#) *AJOG* 2024 doi 10.1016/j.ajog.2023.12.037).

The argument in favour of OTT for extending ovarian function is made for maintaining the health advantages of remaining pre-menopausal rather than extending reproductive potential. This goes to improving the person’s quality of life and reducing the risks of bone density loss and cardiovascular health deterioration.

The points against this line of treatment are:

- The process involves surgical procedures which carry risk, no matter how sophisticated
- Removal of ovarian tissue can reduce endogenous reserves with detrimental consequences
- The actual function and duration of efficacy of the transplant is still unknown

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- The advantages over conventional hormone therapy - oral, transdermal and probably depot - are unproven

*Editorial opinion: What is on offer here is the postponement of a natural process, or will the woman be “feminine forever”? Will she menstruate and possibly ovulate, necessitating other measures to counter unanticipated eventualities? Will these cells age at the same rate as other cells in the woman’s body? Ageing is normal and this means of seeking the fountain of youth seems over-the-top (OTT) to me.*

### Osteoporosis treatment and age

Using data from more than 100,000 participants in randomised trials, it has been established that anti-fracture efficacy of osteoporosis treatments is not age dependent ([Schini et al J Bone Min Res 2024 doi 10.1093/jbmr/zjae040](#)). The researchers compared the impact of various medications on bone mineral density between individuals aged  $\geq 70$  and those  $< 70$  years and found that anti-osteoporosis drugs significantly reduced the risk of fractures in both age groups similarly. This including vertebral, non-vertebral, hip, and all fractures.

The authors concluded that the study demonstrated that anti-osteoporotic medications are effective in reducing the risk of fractures across all ages, with only minor and clinically uncertain differences in fracture risk reduction by age. This finding suggests that the effectiveness of such treatments should not be underestimated in older adults.

### Fezolinetant for VMS

Fezolinetant is a non-hormonal neurokinin 3 receptor antagonist, used for managing moderate-to-severe vasomotor symptoms (VMS). The SKYLIGHT 1 and 2 phase 3 trials explored the effectiveness of either a placebo, 30 mg of fezolinetant, or 45 mg of fezolinetant daily ([Santoro et al Menopause 2024;32:247-57](#)). After 12 weeks, those on placebo were re-randomized to one of the fezolinetant doses, while those already on fezolinetant continued their regimen. The study aimed to evaluate the change in VMS frequency from baseline at week 12, considering various intrinsic (individual-related) and extrinsic (external influence) factors.

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The results demonstrated that the active medication significantly reduced VMS frequency across all examined factors, with notable efficacy in participants who were Black, current smokers, and current alcohol users. The treatment was generally well tolerated, showing comparable rates of treatment-emergent adverse events across all groups.

This finding is significant given the high prevalence of VMS among menopausal women and the need for alternative treatments to hormone therapy, which many are hesitant to use due to concerns about side effects and long-term risks.

The conclusion drawn from these studies is that fezolinetant is an effective and well-tolerated option for treating moderate-to-severe VMS in a diverse population, regardless of the range of lifestyle and phenotypic characteristics. For a more detailed description of the physiology of fezolinetant and a guide to other non-hormonal preparations see [Christ et al](#) (*JAMA* 2023 doi 10.1001/jama.2023.15965).

## Healthy ageing

### Educational achievement

*Menopause Matter's* editor has long been interested in why some people age healthily and enjoy longevity, while others do not. The explanation of "socio-economic status" with its strong correlation to healthy ageing is not a robust factor to accept - as it is too generic, and demands to be explored more rigorously to define which aspects of socio-economic privilege provide the advantage.

It was hoped that a scientific approach to one aspect of socio-economic status (that of educational achievement) could shed light on the key factors that education contributes ([Graf et al](#) *JAMA Netw Open* 2024;7:e240655). The article's main points are:

- Upward educational mobility was significantly associated with a slower pace of aging and a lower risk of death. This slower aging process was quantified using the DunedinPACE epigenetic clock, among others,



and accounted for about half of the observed association between educational mobility and mortality.

- The study supports the notion that interventions aimed at promoting educational attainment could be beneficial in slowing the pace of biological aging and enhancing longevity. This association was consistent across generations and also held true in within-family sibling comparisons.
- The results underscore the potential of epigenetic clocks as near-term measures for the effects of interventions on healthy aging, suggesting that these tools could be instrumental in understanding and mitigating health disparities.

The broader implications of this research highlight the importance of education as a determinant of health, suggesting that educational policies could be a vital component in strategies aimed at promoting healthier aging and reducing mortality risk. The researchers advocate “further experimental research to validate these conclusions and explore the mechanisms through which educational attainment influences biological aging and life expectancy.”

### Optimism & physical functioning

“Attitude is everything” may be a trite slogan but psychologists tell us that a positive outlook is associated with better physical and mental health. Few would disagree, but it is interesting to come across data that quantify higher levels of optimism with higher levels of physical functioning.

6,000 participants in the Women’s Health Initiative study were over the age of 65 years at entry and were diligently followed-up for 6 years, during which time serial measures of their physical abilities were recorded. The researchers showed a correlation between optimism and physical wellbeing over a series of tests ([Koga et al JAMA Psychiatry 2024 doi 10.1001/jamapsychiatry.2023.5068](#)).

These findings beg the question whether optimism is a modifiable state or a stable trait. “States can vary across time as an individual encounters various situations, experiences, and interventions. Traits on the other hand, are stable, intrinsic characteristics of the individual – thus, less likely to be modifiable” according to [Cobert et al \(J Am Ger Society 2022 doi 10.1111/jgs.17958\)](#). Can



interventions change attitudes? Can our own feelings be altered by extrinsic or intrinsic activities or desires? Can we manipulate these factors in our favour?

Can we improve the quality of our lives, and those of our patients, and slow our epigenetic clocks with optimistic attitudes and educational achievement? Can we think our way to a better future?

## Breast cancer screening developments

### Risk estimation

It seems logical to estimate a woman's risk of developing breast cancer so as to tailor both the frequency and age of starting surveillance. One way of doing this is to use family history, the presence of pathogenic variants plus the polygenic risk score (PRS). Using these elements researchers were able to demonstrate "the effectiveness of a breast cancer PRS for risk stratification, alone and combined" ([Mars et al J Clin Onc 2024 doi 10.1200/JCO.23.00295](#)). Prospective research is now awaited to see the effect of such a method in real world situations and its cost effectiveness.

### AI & mammographic prediction

A potential breakthrough in Artificial Intelligence technology named AsymMirai, may be able to predict breast cancer risk up to five years in advance with notable accuracy. It operates by analysing the differences between the left and right breasts, and if proven in the field, it could reduce unnecessary tests, and lead to significant healthcare savings.

This comes at a time in the United States when "One in eight women will develop invasive breast cancer, and 1 in 39 will die from it. Mammograms miss about 20% of breast cancers" ([Marshall Medscape 2024](#)). It is claimed that this advance could assist in the longstanding challenge of integrating AI into cancer detection by improving diagnostic accuracy and personalising screening strategies, and would be particularly beneficial in regions with a shortage of radiologists.

## Alternate treatment for vulvovaginal atrophy

Although the term "vulvovaginal atrophy (VVA)" is seldom used these days, it was the focus of a study comparing the effectiveness of non-invasive

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radiofrequency, vaginal estrogen, and vaginal moisturiser treatments in managing its symptoms ([de Moraes et al Menopause 2024;31:288-302](#)).

32 postmenopausal women received one of the three interventions and the outcomes were evaluated using various measures, including the Vaginal Health Index, Vaginal Maturation Index, a visual scale for VVA symptoms, and the Menopause Rating Scale (MRS) for urogenital symptoms, along with histopathologic analysis of vaginal wall biopsies taken before and after the treatments. After four months, results showed that non-invasive radiofrequency therapy was as effective as vaginal estrogen in treating VVA symptoms and superior to vaginal moisturisers, making it a promising alternative, especially for women who cannot, or prefer not to use estrogen therapy.

### Weight loss with & without MHT

The effects of semaglutide for weight loss on postmenopausal women have not been intensively studied, particularly comparing those who are on menopausal hormone therapy (MHT) and those who are not. A study has been published to evaluate the weight loss response and observe changes in cardiometabolic risk markers among these women ([Hurtado et al Menopause 2024;31:266-74](#)).

The research measured total body weight loss percentage and assessed changes in cardiometabolic risk markers such as glucose levels, blood pressure, and lipids at the 12-month mark. Key findings of the study include:

- The sample comprised 16 women using MHT and 90 not using MHT.
- Women on MHT showed a greater weight loss at all measured intervals (3, 6, 9, and 12 months) compared to those not on MHT, with statistically significant differences at each time point, indicating a better weight loss response in women on MHT.
- At 12 months, a higher proportion of women on MHT achieved both  $\geq 5\%$  and  $\geq 10\%$  weight loss compared to those not on MHT.
- Improvements in cardiometabolic risk markers were observed in both groups.



The study underscores that during the menopause transition, many women experience weight gain and semaglutide treatment in postmenopausal women, especially those on MHT, was associated with an enhanced weight loss response. This finding suggests that MHT may have a synergistic effect with semaglutide in improving weight loss outcomes.

### MHT & depression

Despite the prevalence of depressive symptoms during the menopause transition and the early post-menopause, the effects of MHT on mood-related symptoms remain unclear. A study from a Canadian Clinic was aimed at capturing the effects of any the type of MHT treatment on depressive symptoms ([Gnanasegar et al Menopause 2024;31:320-5](#)).

The findings revealed a two thirds incidence of depressive symptoms among those seeking specialised care, highlighting the burden of depression in this population. The use of MHT was significantly associated with an improvement in depressive symptoms, regardless of whether it was used alone or in conjunction with antidepressant medication. Factors like younger age, lower educational attainment, and smoking were found to correlate with higher depression scores.

The outcome of this study supports the use of MHT as a beneficial treatment for depressive symptoms, suggesting it can play a role in improving the quality of life for those in peri- and postmenopausal years.

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